PATENT COOPERATION TREATY

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From the
INTERNATIONAL PRELIMINARY EXAMINING AUTHORITY

PCT

WRITTEN OPINION

(PCT Rule 66)

To:
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Date of mailing (day/month/year): 19.06.96

Applicant's or agent's file reference: A0619/7001WO

REPLY DUE within 3 months/~~days~~ from the above date of mailing

International application No.	International filing date (day/month/year)	Priority date (day/month/year)
PCT/US 95/11160	01/09/1995	02/09/1994

International Patent Classification (IPC) or both national classification and IPC: A61K39/02

Applicant: BRIGHAM AND WOMEN'S HOSPITAL, INC.

1. This written opinion is the FIRST (first, etc.) drawn up by this International Preliminary Examining Authority.
2. This report contains indications and corresponding pages relating to the following items:
   - I [X] Basis of the opinion
   - II [ ] Priority
   - III [ ] Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
   - IV [ ] Lack of unity of invention
   - V [X] Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
   - VI [X] Certain documents cited
   - VII [X] Certain defects in the international application
   - VIII [X] Certain observations on the international application

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3. The applicant is hereby **invited to reply** to this opinion.

   When? See the time limit indicated above. The applicant may, before the expiration of that time limit, request this Authority to grant an extension, see Rule 66.2(d).

   How? By submitting a written reply, accompanied, where appropriate, by amendments, according to Rule 66.3. For the form and the language of the amendments, see Rules 66.8 and 66.9.

   Also For an additional opportunity to submit amendments, see Rule 66.4. For the examiner's obligation to consider amendments and/or arguments, see Rule 66.4*bis*. For an informal communication with the examiner, see Rule 66.6.

   If no reply is filed, the international preliminary examination report will be established on the basis of this opinion.

4. The final date by which the international preliminary examination report must be established according to Rule 69.2 is: 02/01/1997.

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Authorized officer
Examiner K. Muller-Thomalla
Formalities officer (incl. extension of time limits) Marianne Houyez-Stevens
Telephone No. 8763

Intern. application No.

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I. Basis of the opinion

1. This opinion has been drawn up on the basis of (Substitute sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this opinion as "originally filed".):

[ ] the international application as originally filed.

[x] the description, pages 1,3,5,6,8-18,21-30_____, as originally filed,
pages _____, filed with the demand,
pages 2,4,7,19,20_____, filed with the letter of 06.05.96,

[x] the claims, Nos. _____, as originally filed,
Nos. _____, as amended under Article 19,
Nos. _____, filed with the demand,
Nos. 1-26_____, filed with the letter of 02.04.96,

[ ] the drawings, sheets/fig _____, as originally filed,
sheets/fig _____, filed with the demand,
sheets/fig _____, filed with the letter of _____,

2. The amendments have resulted in the cancellation of:
[ ] the description, pages _____.
[ ] the claims, Nos. _____.
[ ] the drawings, sheets/fig _____.

3. [ ] This opinion has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2(c)):

4. Additional observations, if necessary:

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V. Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step and industrial applicability; citations and explanations supporting such statement

1. STATEMENT

Novelty (N)	Claims 1,4,5,7-14,16-22,24,25,26 (no)_____
	Claims 2,3,6,15,23 (yes)_____
Inventive Step (IS)	Claims 1-26 (no)_____
	Claims _____
Industrial Applicability (IA)	Claims _____
	Claims _____

2. CITATIONS AND EXPLANATIONS

1. The following documents are mentioned for the first time in this written opinion; the numbering will be adhered to in the rest of the procedure:

   D1: Proceedings of the 1994 Meeting of the Anaerobe Society of the Americas, Marina Del Rey, California, USA, July 29-31, 1994. Clinical Infectious Diseases 20 (Suppl.2) 1995, S132-S140,
   D2: Infect. Immun. (1994), 62(8), 3590-3, 1994,
   D3: J. Biol. Chem. (1992), 267(25), 18230-5, 1992
   D4: Infect. Immun. (1991), 59(6), 2075-82, 1991.

2. The Applicant's comments on the prior art documents cited in the International Search Report filed with the letter of 02 April 1996 have been taken into consideration for the establishment of this Written Opinion.

3. According to the Applicant, the claimed invention involves the finding that treatment with a single polymer as defined e.g. in claim 1 can protect against abscess

formation caused by different unrelated live microorganisms.

3.1 In the prior art method according to document D1 (see e.g. abstract; page 138, second column, third paragraph to page 140, table 5), polymer preparations identical to the present ones are used to protect against intraabdominal abscess formation resulting from a challenge with abscess-inducing polymers, such as PS-A, PS-B, or the S. Pneumoniae type 1 capsular polysaccharide. Also known from said document D1 is the fact that the subsequent host response is mediated by the distinct structural and charge motifs associated with the above-mentioned polysaccharides (as also defined in e.g. present claim 1) and is controlled by the cellular immune system.

Thus the only difference between said known immunization method and the present one appears to relate to the original cause of the abscess, which is however not reflected in any of the independent claims relating to methods of protection against abscess formation. Method claims 1 and 25 are thus not novel.

With respect to said difference (causative agent) it would appear that, as it is known that live Bacteroides fragilis as well as specific charge motifs of the latter, play a major role in relation to intraabdominal abscess formation and that in this respect other microorganisms might be active in synergy with B. fragilis or that other factors such as e.g. LPS may also promote intraabdominal abscess formation (see e.g. D3; page 18230, first column, last paragraph to column 2, first paragraph or D4; first three paragraphs of "discussion"), the use of the known polysaccharide preparation of D1 for preventing intraabdominal abscesses which might be formed by one of the above-mentioned other (non

- B. fragilis) microorganisms would also appear to lack an inventive step.

Furthermore, considering that research in the field of pathological intraabdominal abscess formation is likely to be designed in such a way to ultimately find an application in clinical situations and for general therapeutic purposes, the skilled person would consider the polysaccharide preparations of D1 to be an appropriate "medicament" or "pharmaceutical" to prevent intraabdominal abscesses in which B. fragilis or the corresponding specific repeating units and charge motifs play a major role.

Although D1 does not explicitly mention the word "pharmaceutical" for the described polymer preparation (which is identical to the one of the present claims), it is considered that this feature is nonetheless implicitly disclosed in said document.
Thus the present independent claims 11,16,17 and 24, relating to the known polymer per se, as well as to methods for producing the latter, do not satisfy the requirements of Articles 33(2) and 33(3) PCT.

In the above-mentioned independent claims there are thus no precise technical features which enable the distinction between the method for inducing protection, the method for preparing a pharmaceutical, the pharmaceutical preparation (as well as its use) of D1 and the present methods and preparations.
At present the wording of said independent claims is not limited to abscesses formed by heterologeous live organisms. It should be noted that even in the case the latter feature were to be specified, any product claims as well as claims relating to methods of production of said product would still not satisfy the requirements of the PCT, as said feature would be considered to be a

non-limiting functional feature.

3.2 In the light of D1, dependent claims 4,5,7,8,9,10,12,13,14,18,19,20,21 and 22 also appear to lack novelty and inventive step.

3.3 The remaining dependent claims do not appear to contain any additional features which, in combination with the features of any claim to which they refer, involve an inventive step.

3.4 It should be noted that all claims relating to a pharmaceutical containing the above-mentioned polymers and a pharmaceutically acceptable carrier are not novel with respect to any of the further prior art documents cited in the International Search Report which describe such a "pharmaceutical" (see e.g. D2, page 3590, line 1 to page 3591, first paragraph; page 3592, second column, second and third paragraph), even if the latter is used for a different purpose.

In this context it should be noted again that according to the PCT the purpose of a known product does not render the latter novel.

For the assessment of the present "method of treatment" claims 1-10 on the question whether they are industrially applicable, no unified criteria exist in the PCT. The patentability can also be dependent upon the formulation of the claims. The EPO, for example, does not recognize as industrially applicable the subject-matter of claims to the use of a compound in medical treatment, but will allow, however, claims to a known compound for first use in medical treatment and the use of such a compound for the manufacture of a medicament for a new medical treatment.

In this case the claimed uses do not appear to relate to a first medical treatment use.

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VI. Certain documents cited

1. Certain published documents (Rule 70.10)

Application No. Patent No.	Publication date (day/month/year)	Filing date (day/month/year)	Priority date (valid claim) (day/month/year)

Infect. Immun. (1994), 62(11), 4881-6, November 1994

In case the priority date of the present application was not valid, then the above-mentioned document would become relevant in the context of novelty and inventive step.

2. Non-written disclosures (Rule 70.9)

Kind of non-written disclosure	Date of non-written disclosure (day/month/year)	Date of written disclosure referring to non-written disclosure (day/month/year)

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VII. Certain defects in the international application

The following defects in the form or contents of the international application have been noted:

1. To meet the requirements of Rule 5.1(a)(ii) PCT, the documents D1 to D4 should be identified in the description and the relevant background art disclosed therein should be briefly discussed.

2. The attention of the Applicant is drawn to the fact that the application may not be amended in such a way that it contains subject-matter which extends beyond the content of the application as filed, Article 34(2)(b) PCT.

3. In order to expedite further examination you are requested to indicate with your reply the locations in the application as originally filed of the passages forming a basis for the amendments.

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VIII. Certain observations on the international application

The following observations on the clarity of the claims, description, and drawings or on the question whether the claims are fully supported by the description, are made:

1. It is clear from the description and the examples that the causative agent of the abscess (to be ultimately protected from) is essential to the performance of the claimed invention.

   Since none of the independent claims 1,11,16,17,24 or 25 contain this feature they do not meet the requirement following from Article 6 PCT taken in combination with Rule 6(3)(b) PCT that any independent claim must contain all the technical features essential to the invention.

2. The statement in the description at page 30, last paragraph is inconsistent with the definition of the matter for which protection is sought, contrary to Article 84 EPC. The statement should therefore be deleted.

   Furthermore, throughout the description (see e.g. page 4, last paragraph; or page 7, second paragraph to page 8, fourth paragraph etc.) the definition of the present claimed polymer preparations is such that it comprises naturally occurring polysaccharides that include the requisite charged groups. Such a definition renders the scope of the claims unclear and furthermore conflicts with the requirements of Article 33(2) PCT.